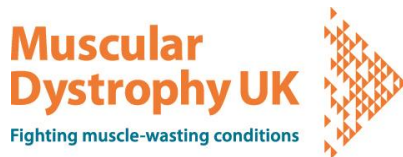


This response was submitted to the Call for Evidence held by the Nuffield Council on Bioethics on *Genome editing* between 27 November 2015 and 1 February 2016. The views expressed are solely those of the respondent(s) and not those of the Council.



Muscular Dystrophy UK's response to Nuffield Council on Bioethics call for evidence: Genome Editing

About Muscular Dystrophy UK

Muscular Dystrophy UK is the charity for 70,000 children and adults living with muscle-wasting conditions. We provide vital information, advice and support to help people live as independently as possible. We accelerate progress in research and drive the campaign for access to emerging treatments.

The charity is on course to invest £1.4million this year (2015/2016) on peer-reviewed, world-class research, to develop potential therapies for muscle-wasting conditions and to improve their management and diagnosis.

About muscle-wasting conditions

Muscular Dystrophy UK covers more than 60 different muscle-wasting conditions. These conditions vary significantly between types, and in many cases, between individuals affected by them – even members of the same family. However, the majority are genetic and cause muscles to weaken and waste over time, resulting in increasing disability. Many affect the heart and respiratory muscles, significantly reducing life-expectancy.

Muscle-wasting conditions may be inherited, as a genetic mutation is passed down the family line. In the case of conditions such as myotonic dystrophy or FSH muscular dystrophy, several generations of a family may be affected. However, the genetic mutations causing muscle-wasting conditions may also appear spontaneously.

There is currently no access to treatments addressing the underlying genetic causes of muscle-wasting conditions in the UK. Interventions such as steroids, physiotherapy, and specialist respiratory and cardiac care are the only options available for protecting and prolonging health and mobility.

About Duchenne and Becker muscular dystrophies, conditions that could be treated with gene-editing

There are approximately 2,500 children adults in the UK affected by Duchenne muscular dystrophy, one of the most severe genetic muscle-wasting conditions. It is caused by genetic mutations in the dystrophin gene, which affects the body's ability to produce this vital muscle protein. The mutation occurs on the 'X' chromosome, meaning the majority of the 100 children born with the condition each year are male. Most will be diagnosed by the age of five, and will be full-time wheelchair-users before the age of twelve. Most will experience life-threatening health complications from their late teens. Life-expectancy remains in the mid-twenties.

Becker muscular dystrophy is also caused by mutations in the dystrophin gene, which, unlike Duchenne muscular dystrophy, do not completely prevent dystrophin production. The result is a similar, yet more slowly progressing condition, affecting a further 2,400 people.

Genome editing to treat muscle-wasting conditions

Genome editing: Professor George Dickson, Royal Holloway, University of London

Muscular Dystrophy UK is currently co-funding a research project in Professor George Dickson's laboratory at Royal Holloway, University of London. The team have developed an innovative gene editing technique with the potential to repair the genetic mutations that cause Duchenne muscular dystrophy. The technique could be the first therapy that offers permanent correction of these genetic mutations.

Professor Dickson's strategy has the potential to permanently correct a genetic mutation in the dystrophin gene. This is done by using enzymes called endonucleases that act like molecular scissors to cut the DNA. These scissors are designed to cut out the precise part of the gene containing the mutation. Other molecular tools are used to add in the correct DNA sequence and join the cut ends together. This would correct the genetic mutation and allow production of the full-size dystrophin protein.

The approach is applicable to all the mutations which cause Duchenne and Becker muscular dystrophies and could also be adapted for the treatment of other neuromuscular conditions.

The technique is conducted in adult muscle cells.

Genome editing: Professor Francesco Muntoni, UCL Institute of Child Health

Muscular Dystrophy UK is also co-funding a three-year project in Professor Francesco Muntoni and Dr Francesco Conti's laboratories at the UCL Institute of Child Health. The aim of the study is to develop the use of gene editing to treat children with Duchenne muscular dystrophy, in cases where the condition is caused by a duplication in exon 2 of the dystrophin gene. For around 10 to 15 percent of people with Duchenne muscular dystrophy, their condition has been caused by exon 2 duplications.

Duplications are very difficult to correct using the experimental therapies that are currently in clinical trials. Prof Muntoni and Dr Conti aim to use genome editing to remove the duplicated DNA copy using 'molecular scissors', potentially leading to an intact gene.

If successful, the dystrophin produced would be fully functional. It would, in effect, be a permanent treatment for Duchenne muscular dystrophy caused by a duplication.

Again, the technique is conducted in adult muscle cells.

Muscular Dystrophy UK's key points on genome editing

- In all discussions surrounding genome editing, it is important to acknowledge the distinction between the manipulation of embryonic cells and of adult muscle cells. It is vital to gain public understanding of the different ways in which gene editing is being used, so that this technique is not only associated with embryonic research.
- We have no ethical concerns for developing genome editing as a potential treatment, targeting adult cells in people with muscle-wasting conditions. The charity also recognises

the potential of using gene editing as a research tool to answer research questions and better understand the underlying biology of muscle-wasting conditions.

- We would consider supporting research involving the use of gene editing research in embryos, if this is used as a research tool (not a means of direct treatment), and is conducted within an appropriate regulatory and ethical framework.
- Using genome editing on embryos to treat genetic disease would require an IVF step, in order to create the embryo and modify it to correct the genetic fault. However, this relies on prior knowledge of family history of a genetic disease. In a substantial number of cases the genetic mutation is spontaneous. When a family history of a genetic condition does exist, in the case of many conditions there is currently a viable IVF method in use, in the form of pre implementation genetic diagnosis. If a woman or man is aware they are a carrier of a muscle-wasting condition, IVF allows the selection of healthy embryos for implantation. Therefore, in our view, the use of genome editing techniques in embryos to prevent inheritance of muscle-wasting conditions is unnecessary.
- Genome editing offers enormous potential for the future of research, but we believe it is vital that all further development of the technique takes place within the appropriate regulatory and ethical frameworks. Furthermore, thorough, clear dialogue must take place in the public space on the future use of gene-editing to treat genetic diseases.